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Honey Used in Medicinal Preparation

A vast new honey market may be opening in the field of pharmaceutical preparations. The following report lists the various medicines in which honey has been used successfully as a vehicle. It also reports on the quality requirements honey producers and packers must take into consideration if they expect to supply pharmaceutical firms.

By DRS. ALFONSO R. GENNARO, CATHERINE N. SIDERI, NATHAN RUBIN and ARTHUR OSOL
School of Chemistry, Philadelphia College of Pharmacy and Science

HONEY HAS NOT been used in modern medicinal products manufacture to the extent that might be expected from the many references to medicinal uses of honey in the older literature. In present-day practice, the pharmaceutical manufacturer must be assured of the long-term stability of his products, for these may remain in distribution channels for many months before they are consumed. When a product contains fermentable sugars, as is the case when honey is an ingredient, two types of stability problems are involved: the chemical stability of the active ingredient or ingredients, and the microbiologic stability of the preparation as a whole. Very little information that may be helpful to the pharmaceutical manufacturer in answering these questions about the stability of honey-containing medicinals has been available. Furthermore, the manufacturer would want to have assurance that successive shipments of honey would have the same, essentially uniform, quality so that his product would always be the same; for this purpose he would expect certain specifications to be applicable.

To provide the required information a two-year study of the utility of honey as an ingredient of medicinal products was performed at the School of Chemistry of the Philadelphia College of Pharmacy and Science under a contract with the U.S. Department of Agriculture.* The results of the study are briefly summarized in this paper.

* A report of work done under contract with the U.S. Department of Agriculture and authorized by the Research and Marketing Act of 1946. The contract is being supervised by the Eastern Utilization Research and Development Division of the Agricultural Research Service.

Chemical Stability Studies

Vitamins - Honey solutions of the common water-soluble vitamins were studied under various conditions of preparation and storage, the vitamins being thiamine (vitamin B1), riboflavin (vitamin B2), cyanocobalamin (vitamin B12), and ascorbic acid (vitamin C). Only riboflavin, used in the form of sodium riboflavin-5′-phosphate, and a combination of riboflavin and thiamine showed long-term stability in honey solutions, when these were stored in brown bottles. Honey would be, however, an excellent vehicle for making vitamin solutions, as on a physician's prescription, that are to be consumed within two or three weeks.

Ferrous Sulfate - One of the popular iron tonics is Ferrous Sulfate Syrup, made by dissolving ferrous sulfate in sugar syrup flavored with peppermint. A similar preparation may be made (omitting the peppermint) with honey as the vehicle; this is very palatable, free of the metallic after-taste characteristic of most preparations containing iron, and stable (no change occurred in the period of 11 months during which it was tested).

Sulfonamides - The "sulfa" drugs are very important drugs, and large quantities of liquid "suspensions" of them are used. In particular, mixtures of sulfadiazine, sulfamerazine, and sulfamethazine are advantageous, and suspensions of these "sulfa" drugs in a vehicle composed largely of honey were studied. Such suspensions turned out to be very stable, easily mixed, and ex-

ceptionally palatable; honey is decidedly advantageous in these medicinal products.

Preparations for Cough - Here, too, honey was found to be an excellent vehicle. Two formulations, containing an antihistaminic agent and either dihydrocodeinone or codeine, besides other ingredients commonly used in cough medicines, were found to be palatable, stable, and effective. Honey is an eminently satisfactory vehicle for this class of medicinal products.

Aspirin - A stable and palatable liquid preparation of aspirin has long been sought and it was hoped that honey might be the long-sought vehicle. Long-term stability was not attained with any of the formulations of aspirin prepared in this study, but it was found that "extemporaneous" preparations, ideal for administration to infants and children, deteriorated to the extent of only five per cent in two days.

Preservation Against Microbiological Deterioration

Preparations of honey which contain also water are prone to deterioration by microbiological organisms. How to prevent this was one of the main problems investigated in this study. Solutions of honey and water were deliberately contaminated with various organisms - **Bacillus subtilis, Proteus vulgaris,** and **Penicillium notatum.** Of the various preservatives tested, sorbic acid completely prevented microbiological deterioration when used in a concentration of 0.05 per cent (weight-in-volume).

Quality Specifications for Honey

Various floral types of honey were used in this study, all described as having been heat-processed and filtered. Some of the samples, however, required filtration, others being so clear that this treatment was not needed, a matter of considerable advantage to manufacturers who may find filtration of honey to be a cumbersome procedure. In those instances where filtration was necessary Celite Standard Super-Cel was used as a filter-aid, in amounts of 0.5 to 0.75 per cent, and the filtration was performed under 10 to 14 pounds of pressure. The following specifications for honey suitable for use in medicinal products are recommended:

General Description - Honey is the nectar of floral exudations of plants gathered and stored in the comb by honeybees Apis mellifera Linne (Fam. Apidae). It must be heat treated for 30 minutes [140°F.-160°F. (maximum)] and free from foreign substances such as parts of insects, leaves, etc., but may contain pollen grains. When graded according to the United States Standards for Grades of Extracted Honey (18 F.R. 52.1391 - 52.1404), it must be classified as "U.S. Choice" or "U.S. Fancy".

Moisture Content - Not more than 18.6 per cent, by weight. This corresponds to a refractive index (nD20°) of not less than 1.4900, and a specific gravity (20°/20°C.) of not less than 1.4129.

Optical Rotation - Honey is levorotatory at 20°C.

Residue on Ignition - Not more than 0.40 per cent.

Artificial Honey - Introduce 10 ml. of a mixture of equal volumes of honey and water into a test tube and add 5 ml. ether. Shake gently and allow to stand until the ether layer is clear. Transfer 2 ml. of this clear ether solution to a small test tube and add a large drop of freshly prepared resorcinol solution (1 Gm. resorcinol in 100 ml. of hydrochloric acid of sp. gr. 1.18 - 1.19. A cherry-red color appearing within one minute indicates the presence of artificial honey. Yellow to salmon shades have no significance.

Acidity - A solution of 10 Gm. of honey in 50 ml. of water requires not more than 5.0 ml. of 0.1N sodium hydroxide for neutralization, using phenolphthalein as indicator.

Color - Shall not be darker than Light Amber, when determined by use of the U.S.D.A. permanent glass color standards.

Floral Type - At the discretion of the manufacturer. (The addition of therapeutic agents to honey might alter its taste, and it appears advisable to leave the choice of the floral type to the manufacturer. Regardless of the floral type selected, the honey should meet all other specifications).

Packaging and Storage - Honey should be stored in well-closed containers, and the temperature should not exceed 90°F. for a prolonged period. Honey that has granulated may be liquefied in its container by heating at a temperature not over 160°F. for 30 minutes, with occassional stirring.

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